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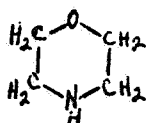
SUBJECT: PP# 5F1606. Dual on corn. Question of metabolites containing the morpholine moiety. DATE: **AUG 13 1976**

FROM: Donald Reed, Chemist, Chemistry Branch
Registration Division (WH-567)

TO: Product Manager # 24 (Jacoby)
and Toxicology Branch

THRU: Chief, Chemistry Branch

As is shown in the attached Figure, two of the postulated metabolites of Dual (CGA-24705) contain a ring structure similar to that of morpholine.



These compounds are Compounds J and X in Figure 1. Direct evidence of the presence of either of these compounds was not found in either the plant or animal metabolism studies. However, since the metabolism studies employed labeling in the phenyl ring, evidence of any nitrogen-containing compounds formed by fission of the nitrogen-phenyl bond would not have been apparent (other than the presence of phenols showing that the nitrogen side chain had split off).

The possibility of forming morpholine (which is of toxicological concern) from Dual or its metabolites is extremely remote. Three rather unlikely reactions would need to occur to result in the formation of morpholine: (1) ring closure in the acetamide portion of the molecule; (2) fission of the N-phenyl bond; and (3) reduction of the morpholinone moiety to morpholine.

No evidence of the occurrence of Step 1 was detected in the metabolism studies. The partial formation of compound X (CGA-49751) in the analytical method is preceded by 16 hours of refluxing with 6 N HCl, i.e. very severe conditions.

Step 2, fission of the N-phenyl bond, is less likely than fission of either of the N-alkyl bonds, e.g. formation of an aniline is more likely than formation of the phenol in this class of compounds (aniline is a precursor of the phenol).

Even should Steps 1 and 2 occur, the resulting compound would not be the secondary amine, morpholine; it would be morpholinone. Conversion of morpholinone to morpholine would be expected to require rather stringent reducing conditions.

Conclusions and Recommendation

The unlikelihood of the above steps occurring, plus the showing that no real residues of the expected parent compound and metabolites result in corn grain from this preemergent use, allow us to conclude that residues of morpholine would not be a problem resulting from this use of Dual.

However, should the petitioner seek a tolerance in the future for real residues of Dual on a direct human food item, we should request that specific information be provided to show whether morpholine or closely related compounds containing the morpholine moiety, could result from such a use. Ciba-Geigy should be advised of this decision.

Donald Reed